

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet	1	of	2
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**Complete if Known**

<b>Application Number</b>	10/621,229
<b>Filing Date</b>	July 15, 2003
<b>First Named Inventor</b>	Legarda Ibanez
<b>Art Unit</b>	1614-167
<b>Examiner Name</b>	Jennifer Kim
<b>Attorney Docket Number</b>	55979/314589 (0100US)

## U.S. PATENT DOCUMENTS

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## FOREIGN PATENT DOCUMENTS

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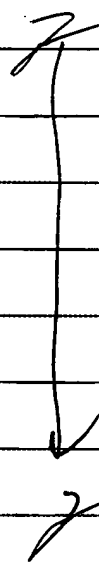
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		Application Number	10/621,229
		Filing Date	July 15, 2003
		First Named Inventor	Legarda Ibanez
		Art Unit	3644 / 617
		Examiner Name	Jennifer Kim
		Attorney Docket Number	55979/314589 (0100US)
Sheet	2	of	2

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1	American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Washington, D.C., American Psychiatric Association, 1994, pp. 194-204.	
	2	BUCK, K. J., Reversal of Alcohol Dependence and Tolerance by a Single Administration of Flumazenil, The Journal of Pharmacology and Experimental Therapeutics, 1991, Vol. 257, No. 3, pp. 984-989.	
	3	FILE, S.E., Effects of Nitrendipine, Chlordiazepoxide, Flumazenil and Baclofen on the Increased Anxiety Resulting from Alcohol Withdrawal, Prog. Neuro-Psychopharmacol & Biol. Psychiatry, 1992, Vol. 16, No. 1, pp. 87-93.	
	4	GERRA, G., Effectiveness of Flumazenil in the Treatment of Ethanol Withdrawal, Current Therapeutic Research, July 1991, Vol. 50, No. 1, pp. 62-66.	
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	7	POTOKAR, J., Flumazenil in Alcohol Withdrawal: a Double-blind Placebo-controlled Study, Alcohol & Alcoholism, 1997, Vol. 32, No. 5, pp. 605-611.	
	8	Practice Management Information Corporation: International Classification of Diseases, 9 <sup>th</sup> Revision, Clinical Modification, Sixth Edition (ICD-9-CM), 2004, selected pages.	

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		Group Art Unit	4614 / 617
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<b>OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS</b>			
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J	3.	Bell, E.C., <i>et al.</i> , "Response to Flumazenil in the Late Luteal Phase and Follicular Phase of the Menstrual Cycle in Healthy Control Females," <i>Psychopharmacology</i> , Vol. 172, pp. 248-254 (2004)	
	4.	Berezhnoy, D., <i>et al.</i> , "Conformational Changes at Benzodiazepine Binding Sites of GABA <sub>A</sub> Receptors Detected With a Novel Technique," <i>J. Neurochemistry</i> , Vol. 92, pp. 859-866 (2005)	
	5.	Betz, C., <i>et al.</i> , "Could a Common Biochemical Mechanism Underlie Addictions?," <i>J. Clin. Pharm. Ther.</i> , Vol. 25, No. 1, pp. 11-20 (2000) (Abstract Only)	
	6.	Biggio, G., <i>et al.</i> , "Molecular Mechanisms of Tolerance to and Withdrawal of GABA(A) Receptor Modulators," <i>Eur. Neuropsychopharmacol.</i> , Vol. 13, No. 6, pp. 411-423 (2003)	
	7.	Boehm, S.L., <i>et al.</i> , "γ-Aminobutyric Acid A Receptor Subunit Mutant Mice : New Perspectives on Alcohol Actions," <i>Biochemical Pharmacology</i> , Vol. 68, pp. 1581-1602 (2004)	
	8.	Buckley, S.T., <i>et al.</i> , "GABA <sub>A</sub> Receptor β Subunit mRNA Expression in the Human Alcoholic Brain," <i>Neurochemistry International</i> , Vol. 45, pp. 1011-1020 (2004)	
	9.	Casasola, C., <i>et al.</i> , "Hyperexcitability Induced by GABA Withdrawal Facilitates Hippocampal Long-term Potentiation," <i>Neuroscience</i> , Vol. 126, pp. 163-171 (2004)	
	10.	Clark, M., "Sensitivity of the Rat Hippocampal GABA <sub>A</sub> Receptor α4 Subunit to Electroshock Seizures," <i>Neuroscience Letters</i> , Vol. 250, pp. 17-20 (1998)	
	11.	Criswell, H.E., <i>et al.</i> , "Effect of Zolpidem on Gamma-aminobutyric Acid (GABA)-Induced Inhibition Predicts the Interaction of Ethanol with GABA on Individual Neurons in Several Rat Brain Regions," <i>J. Pharmacol. Exp. Therp.</i> , Vol. 273, No. 1, pp. 526-536 (1995) (Abstract Only)	
	12.	Davies, M., "The Role of GABA <sub>A</sub> Receptors in Mediating the Effects of Alcohol in the Central Nervous System," <i>J. Psychiatry Neurosci.</i> , Vol. 28, No. 4, pp. 263-274 (2003)	
J	13.	Devaud L.L., <i>et al.</i> , "Bidirectional Alterations of GABA(A) Receptor Subunit Peptide Levels in Rat Cortex During Chronic Ethanol Consumption and Withdrawal," <i>J. Neurochem.</i> , Vol. 69, No. 1, pp. 126-130 (1997) ; (Abstract only)	


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		First Named Inventor	Juan Ibanez
		Group Art Unit	1614 1617
		Examiner Name	Jennifer Kim
Sheet 3	of 10	Attorney Docket Number	55979-314589 (55979-0100)

OTHER INFORMATION - NON PATENT LITERATURE DOCUMENTS			
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7	14.	Devaud L.L., <i>et al.</i> , "Chronic Ethanol Consumption Differentially Alters the Express of Gamma-aminobutyric acid <sub>A</sub> ...Chain Reaction Analysis," <i>Mol. Pharmacol.</i> , Vol. 48, No. 5, pp. 861-868 (1995); <i>Abstract only</i>	
	15.	Devaud L.L., <i>et al.</i> , "Influence of Gender on Chronic Ethanol-Induced Alterations in GABA <sub>A</sub> Receptors in Rats," <i>Brain Res.</i> , Vol. 796, Nos. 1&2, pp. 222-230 (1998); <i>Abstract only</i>	
	16.	Devaud L.L., <i>et al.</i> , "Sensitization of Gamma-Aminobutyric acid <sub>A</sub> Receptors to Neuroactive Steroids in Rats During Ethanol Withdrawal," <i>J. Pharmacol. Exp. Ther.</i> , Vol. 278, No. 2, pp. 510-517 (1996); <i>Abstract only</i>	
	17.	DuBois, D.W., <i>et al.</i> , "Binge Ethanol Exposure Delays Development of GABAergic Miniature Postsynaptic Currents in Septal Neurons," <i>Developmental Brain Research</i> , Vol. 152, pp. 199-212 (2004)	
	18.	File, S.E., <i>et al.</i> , "Effects of Nitrendipine, Chlordiazepoxide, Flumazeil and Baclofen on the Increased Anxiety Resulting from Alcohol Withdrawal," <i>Prog. Neuropsychopharmacol. Biol. Psychiatry</i> , Vol. 16, No. 1, pp. 87-93 (1992) (Abstract Only)	
	19.	File, S.E., <i>et al.</i> , "Benzodiazepine Withdrawal: Behavioural Pharmacology and Neurochemical Changes." <i>Biochem. Soc. Symp.</i> , Vol. 59, pp. 97-106 (1993) (Abstract Only)	
	20.	File, S.E., <i>et al.</i> , "Flumazenil but not Nitrendipine Reverses the Increased Anxiety During Ethanol Withdrawal in the Rat," <i>Psychopharmacology</i> , Vol. 98, No. 2, pp. 262-264 (1989); <i>Abstract only</i>	
	21.	Finn, D.A., <i>et al.</i> , "Differential Change in Neuroactive Steroid Sensitivity During Ethanol Withdrawal," <i>J. Pharmacology and Experimental Therapeutics</i> , Vol. 292, No. 1, pp. 394-405 (2000)	
	22.	Follesa, P., <i>et al.</i> , "Modulation of GABA <sub>A</sub> receptor Gene Expression by Allogpregnanolone and Ethanol," <i>Euro. J. Pharmacology</i> , Vol. 500, pp. 413-425 (2004)	
	23.	Follesa, P., <i>et al.</i> , "γ-Hydroxybutyric Acid and Diazepam Antagonize a Rapid Increase in GABA <sub>A</sub> Receptors α4 Subunit mRNA Abundance Induced by Ethanol Withdrawal in Cerebellar Granule Cells," <i>Molecular Pharmacology</i> , Vol. 63, No. 4, pp. 896-907 (2003)	
7	24.	Green, K.L., <i>et al.</i> , "The Influence of Menstrual Cycle Phase on Sensitivity to Ethanol-Like Discriminative Stimulus Effects of GABA <sub>A</sub> -Positive Modulators," <i>Pharmacology Biochemistry and Behavior</i> , Vol. 64, No. 2, pp. 379-383 (1999)	

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Z	25.	Grobin, A.C., <i>et al.</i> , "The role of GABA(A) Receptors in the Acute and Chronic Effects of Ethanol," <i>Psychopharmacology</i> (Berl.), Vol. 139, Nos. 1-2, pp. 2-19 (1998) (Abstract Only)		
	26.	Grobin, A.C., <i>et al.</i> , "Chronic Ethanol Administration Alters Immunoreactivity for GABA <sub>A</sub> Receptor Subunits in Rat Cortex in a Region-Specific Manner," <i>Alcoholism</i> , Vol. 24, No. 8, pp. 1137-1144 (2000); <i>Abstract only</i>		
	27.	Hanchar, H.J., <i>et al.</i> , "Alcohol Effects on $\gamma$ -aminobutyric Acid Type A Receptors: Are Extrasynaptic Receptors the Answer?," <i>Life Sciences</i> , Vol. 76, pp. 1-8 (2004)		
	28.	Hirani, K., <i>et al.</i> , "Evaluation of GABAergic Neuroactive Steroid 3 $\alpha$ -hydroxy-5 $\alpha$ -pregnane-20-one as a Neurobiological Substrate for the Anti-Anxiety Effect of Ethanol in Rats," <i>Psychopharmacology</i> (Berl.), (Epub ahead of print) (2005) (Abstract Only)		
	29.	Holtman, Jr., J.R., <i>et al.</i> , "Modification of Morphine Analgesia and Tolerance by Flumazenil in Male and Female Rats," <i>Euro. J. Pharmacology</i> , Vol. 470, pp. 149-156 (2003)		
	30.	Janak, P.H., <i>et al.</i> , "The Reinforcing Effects of Ethanol are Altered by the Endogenous Neurosteroid, Allopregnanolone," <i>Alcohol Clin. Exp. Res.</i> , Vol. 22, No. 5, pp. 1106-1112 (1998) (Abstract Only)		
	31.	Janis, G.C., <i>et al.</i> , "Effects of Chronic Ethanol Consumption and Withdrawal on the Neuroactive Steroid 3 $\alpha$ -hydroxy-5 $\alpha$ -pregnane-20-one in Male and Female Rats," <i>Alcohol Clin. Exp. Res.</i> , Vol. 22, No. 9, pp. 2055-2061 (1998) (Abstract Only)		
	32.	June, H.L., <i>et al.</i> , "Ethanol Self-Administration in Freely Feeding and Drinking Rats; Effects of Ro15-4513 alone, and in Combination with Ro15-1788 (Flumazenil)," <i>Psychopharmacology</i> (Berl.), Vol. 115, No. 3, pp. 332-339 (1994) (Abstract Only)		
	33.	Kang, M., <i>et al.</i> , "Persistent Reduction of GABA(A) Receptor-Mediated Inhibition in Rat Hippocampus After Chronic Intermittent Ethanol Treatment," <i>Brain Res.</i> , Vol. 709, No. 2, p. 221-228 (1996) (Abstract Only)		
	34.	Kang, M., <i>et al.</i> , "Alteration in the Sensitivity of GABA(A) Receptors to Allosteric Modulatory Drugs in Rat Hippocampus After Chronic Intermittent Ethanol Treatment," <i>Alcohol Clin. Exp. Res.</i> , Vol. 22, No. 9, p. 2165-2173 (1998) (Abstract Only)		
✓	35.	Knapp, D.J., <i>et al.</i> , "SB242084, Flumazenil, and CRA1000 Block Ethanol Withdrawal-Induced Anxiety in Rats," <i>Alcohol</i> , Vol. 32, pp. 101-111 (2004)		
Z	36.	Ma, L., <i>et al.</i> , "Transcriptional Regulation of the Mouse Gene Encoding the $\alpha$ -4 Subunit of the GABA <sub>A</sub> Receptor," <i>J. Biological Chemistry</i> , Vol. 279, No. 39 pp. 40451-40461 (2004)		
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		Group Art Unit	1614- 1617
		Examiner Name	Jennifer Kim
Sheet 5	of 10	Attorney Docket Number 55979-314589 (55979-0100)	

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J	37.	Mahmoudi, M.K., <i>et al.</i> , "Chronic Intermittent Ethanol Treatment In Rats Increases GABA (A) Receptor Alpha4-subunit Expression: Possible Relevance to Alcohol Dependence," <i>J. Neurochem.</i> , Vol. 68, No. 6, pp. 2485-2492 (1997) (Abstract Only)	
	38.	Mann, K., "Pharmacotherapy of Alcohol Dependence," <i>CNS Drugs</i> , Vol. 18, No. 8, pp. 485-504 (2004)	
	39.	Matthews, D.B., <i>et al.</i> , "Differential Regulation of GABA(A) Receptor Gene Expression by Ethanol in the Rat Hippocampus Versus Cerebral Cortex," <i>J. Neurochem.</i> , Vol. 70, No. 3, pp. 1160-1166 (1998) (Abstract Only)	
	40.	Mitsuyama, H., <i>et al.</i> , "GABA(A) Receptor Alpha1, Alpha4, and Beta3 Subunit mRNA and Protein Expression in the Frontal Cortex of Human Alcoholics," <i>Alcohol Clin. Exp. Res.</i> , Vol. 22, No. 4, pp. 815-822 (1998) (Abstract Only)	
	41.	Moy, S.S., <i>et al.</i> , "Enhanced Ultrasonic Vocalization and Fos Protein Expression Following Ethanol Withdrawal: Effects of Flumazenil," <i>Psychopharmacology</i> , Vol. 152, pp. 208-215 (2000)	
	42.	Moy, S.S., <i>et al.</i> , "Flumazenil Blockade of Anxiety Following Ethanol Withdrawal in Rats," <i>Psychopharmacology</i> , Vol. 131, pp. 354-360 (1997)	
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	44.	Sanna, E., <i>et al.</i> , "Changes in GABA <sub>A</sub> Receptor Gene Expression Associated with Selective Alterations in Receptor Function and Pharmacology After Ethanol Withdrawal," <i>J. of Neuroscience</i> , Vol. 23, No. 37, pp. 11711-11724 (2003)	
	45.	Savic, I., <i>et al.</i> , "Feasibility of Reversing Benzodiazepine Tolerance with Flumazenil," <i>Lancet</i> , Vol. 337, pp. 133-137 (1991)	
	46.	Schmitt, U., <i>et al.</i> , "Free-choice Ethanol Consumption Under the Influence of GABAergic Drugs in Rats," <i>Alcohol Clin. Exp. Res.</i> , Vol. 26, No. 4, pp. 457-462 (2002) (Abstract Only)	
J	47.	Stanley, K.M., <i>et al.</i> , "Impact of an Alcohol Withdrawal Syndrome Practice Guideline on Surgical Patient Outcomes," <i>Pharmacotherapy</i> , Vol. 23, No. 7, pp. 843-854 (2003) (Abstract Only)	


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7	48.	Sundstrom-Poromaa, I., <i>et al.</i> , "Hormonally Regulated $\alpha_4\beta_2\delta$ GABA <sub>A</sub> Receptors are a Target for Alcohol," <i>Nature Neuroscience</i> , Vol. 5, No. 8, pp. 721-722 (2002)	
	49.	Uzbay, I.T., <i>et al.</i> , "Effects of Flumazenil on Ethanol Withdrawal Syndrome in Rats," <i>Arzneimittelforschung</i> , Vol. 45, No. 2, pp. 120-124 (1995) (Abstract Only)	
	50.	Vanover, K.E., <i>et al.</i> , "Positive Allosteric Modulators of the GABA <sub>A</sub> Receptor: Differential Interaction of Benzodiazepines and Neuroactive Steroids With Ethanol," <i>Psychopharmacology</i> , Vol. 141, pp. 77-82 (1999)	
	51.	Vanover, K.E., "Effects of Benzodiazepine Receptor Ligands and Ethanol in Rats Trained to Discriminate Pregnanolone," <i>Pharmacology, Biochemistry and Behavior</i> , Vol. 67, pp. 483-487 (2000)	
	52.	Verheul, R., <i>et al.</i> , "A Three-Pathway Psychobiological Model of Craving for Alcohol," <i>Alcohol &amp; Alcoholism</i> , Vol. 34, No. 2, pp. 197-222 (1999)	
	53.	Weinbroum, A., <i>et al.</i> , "Flumazenil Potentiation of Postoperative Morphine Analgesia," <i>Clin. J. Pain</i> , Vol. 16, No. 3, pp. 193-199 (2000) (Abstract Only)	
	54.	White, J., <i>et al.</i> , "Antagonism of a Nicotine Plus Midazolam Discriminative Cue in Rats," <i>Behav. Pharmacol.</i> , Vol. 5, No. 3, pp. 351-355 (1994) (Abstract Only)	
	55.	Van Miert, AS, "Appetite-Modulating Drugs in Dwarf Goats, With Special Emphasis on Benzodiazepine-Induced Hyperphagia and its Antagonism by Flumazenil and RO 15-3505", <i>J. Vet Pharmacol Ther.</i> , Jun; 12(2):147-56 (1989) ; <i>Abstract only</i>	
2	56.	Zheng, T.M., <i>et al.</i> , "Chronic Flumazenil Alters GABA(A) Receptor Subunit mRNA Expression, Translation Product Assembly and Channel Function in Neuronal Cultures," <i>J. Pharmacol. Exp. Ther.</i> , Vol. 277, No. 1, pp. 525-533 (1996) (Abstract Only)	

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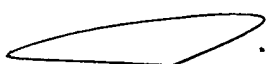
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F	57.	Baldwin, H.A., <i>et al.</i> , "Flumazenil Prevents the Development of Chlordiazepoxide Withdrawal in Rats Tested in the Social Interaction Test of Anxiety," <i>Psychopharmacology</i> , Vol. 97, No. 3, pp. 424-426 (1989) (Abstract Only)	
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		Filing Date	July 15, 2003
		First Named Inventor	Juan Ibanez
		Group Art Unit	1614-1617
		Examiner Name	Jennifer Kim
Sheet 8 of 10	Attorney Docket Number	55979-314589 (55979-0100)	

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Z	68.	Holt, R.A., <i>et al.</i> , "Chronic Treatment with Diazepam or Abecarnil Differently Affects the Expression of GABA <sub>A</sub> Receptor Subunit mRNAs in the Rat Cortex," <i>Neuropharmacology</i> , Vol. 35, Nos. 9 & 10, pp. 1457-1463 (1996); <i>Abstract only</i>	
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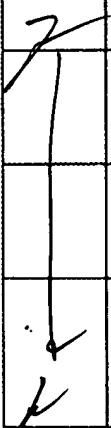
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	76.	Adkins, C.E., <i>et al.</i> , "α <sub>4</sub> β <sub>3</sub> δ GABA <sub>A</sub> Receptors Characterized by Fluorescence Resonance Energy Transfer-derived Measurements of Membrane Potential," <i>J. Biological Chemistry</i> , Vol. 276, No. 42, pp. 38934-38939 (2001)	
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	88.	Sedvall, G., <i>et al.</i> , "Recent Advances in Psychiatric Brain Imaging," <i>Acta Radiol. Suppl.</i> , Vol. 374, pp. 113-115 (1990) (Abstract Only)	

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